

Module 4: Case Investigation of Avian Influenza



Learning Objectives

- Describe the objectives and steps of a A(H5) outbreak investigation
- Conduct an investigation of human A(H5N1) case/cluster
- Describe how to communicate investigation findings

Case Investigation Module Format

- **Interactive case studies and instructional slides**
- **Rapid response team (RRT) investigation of avian influenza cluster or case**
- **Evaluation of an RRT avian influenza investigation**
- **Conduct investigation in groups**

Overview of investigation of human A(H5N1) case/cluster

- **Pre-Investigation**
 - Planning the Response
- **Investigation**
 - Confirm case/cluster
 - Interviewing
 - Specimen Collection
 - Contact Identification
 - Assessing Transmission
 - Case Finding
 - Data Management / creating an Epidemic Curve
 - Reporting / writing a Summary Report
 - Implement control measures
- **After the Investigation**
 - Evaluate Performance

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Pre-Investigation

Before you leave to investigate

Pre-Investigation: Gather Preliminary Information

Assess the situation

- **Information to collect:**
 - Number of suspected cases
 - Geographic location of cases
 - Date of onset of cases
 - Signs and symptoms
 - Exposure history – contact with birds, travel, occupational
 - Lab tests
 - Cases reported in birds
- **Consider the security, weather, accommodation, etc. situations in the area**

Pre-Investigation: Plan the Response

- **Bring RRT together**
 - Refer to Team Composition module for roles and responsibilities of RRT members
- **Discuss each person's roles and responsibilities : “functions more important than persons”**
- **Don't delay forever in order to get the “dream team”**

Pre-Investigation: Documentation

- Information already gathered
- List of contacts with their details
- Forms: case reporting, lab, etc.
- Case definitions
- Standardized questionnaires
- Standard Operating Procedures / Guidelines
 - Case management
 - Laboratory
 - Infection Protection Control (IPC)
- Educational material
 - Influenza safety brochures and posters
 - Easy to read / pictures
 - Will require adaptation

Pre-Investigation: Resources

- **People**
 - Local health workers caring for case-patient
 - Veterinarians, clinical and laboratory experts, support personnel
- **Ministry of Health**
 - Advice, guidance, additional personnel
- **World Health Organization (WHO), FAO**
- **Other:**
 - Transportation
 - Security
 - Communication devices, IT...
 - Money

Pre-Investigation: Supplies

- **Epidemiological**
 - Notebook (or laptop) for recording data
 - Pencil, graph paper ,rubber
- **Medical**
 - Antiviral medication
- **Laboratory**
 - Specimen collection materials
 - Transportation containers
 - Cold chain
 - Viral transport media
- **Personal Protective Equipment (PPE)**

Pre-Investigation: Supplies

- **PPE**
 - Masks, gloves, gown, cap, goggles, aprons, shoe covers / boots
- **Desinfection**
 - Solution for desinfection
 - Sprayers

Don't delay forever in order to get all the perfect supplies and conditions

Pre-Investigation: Sectors to be informed

- **Government Officials**
- **Health Authorities**
- **Veterinary Health Authority**
- **Laboratory (specimen maybe send)**
- **Non-governmental organizations**
- **International organizations**

Rapid Response Team (RRT) Investigation

Objectives of H5N1 Case/Cluster Investigation

- **Assess the possibility of human-to-human transmission**
- **Stop or slow the spread of pandemic influenza at the source (e.g. rapid containment)**
- **Minimize mortality and morbidity**

Steps of Investigation

1. **Confirm existence of case/cluster**
2. **Collect samples for laboratory tests**
3. **Identify and follow-up contacts**
4. **Characterize the outbreak (descriptive epidemiology : TPP)**
5. **Investigate reservoir or source of infection (H2H)**
6. **Conduct active case finding**
7. **Implement immediate control measures : containment?**
8. **Report to authorities**

Investigating a Suspect Case/Cluster

Evidence for H5N1 infection based on:

- **Clinical findings**
- **Evidence of Epidemiological link / Exposure**
- **Laboratory results**

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1. Case Definitions

Case Definitions

- **“Standardizes” the investigation**
- **Clear criteria**
 - Signs
 - Symptoms
 - Lab results
- **Objective measures if feasible**
- **Easy to understand**
- **Easy to use in the field**

WHO Case Definition for avian influenza A(H5N1)

- Person under investigation
- Suspected Case
- Probable Case
- Confirmed Case

Person Under Investigation

Person whom public health authorities have decided to investigate for possible H5N1 infection

Suspect Case

Acute lower respiratory illness with fever ($>38^{\circ}\text{C}$) and cough, shortness of breath, or difficulty breathing;

AND

1 or more of the following exposures in the 7 days prior to symptom onset:

Suspect Case: exposures

- Close contact (within 1 metre) with a **person** (e.g. caring for, speaking with, or touching) who is a suspected, probable, or confirmed H5N1 case;
- Exposure (e.g. handling, slaughtering, defeathering, butchering, preparation for consumption) to **poultry** or **wild birds** or their remains or to environments contaminated by their faeces in an area where H5N1 infections in animals or humans have been suspected or confirmed in the last month;
- **Consumption** of **raw** or undercooked **poultry products** in an area where H5N1 infections in animals or humans have been suspected or confirmed in the last month;
- Close contact with a **confirmed H5N1 infected animal** other than poultry or wild birds (e.g. cat or pig);
- Handling **samples** (animal or human) suspected of containing H5N1 virus in a laboratory or other setting.

Probable Case

- **Probable definition 1:**
 - A person meeting the criteria for a suspected case AND one of the following additional criteria:
 - infiltrates or evidence of an acute pneumonia on chest **radiograph** plus evidence of respiratory failure (hypoxemia, severe tachypnea)
 - OR
 - positive **laboratory** confirmation of an influenza A infection but insufficient laboratory evidence for H5N1 infection.
-
- **Probable definition 2:**
 - A person **dying** of an unexplained acute respiratory illness who is considered to be epidemiologically linked by time, place, and exposure to a probable or confirmed H5N1 case.

Confirmed Case

A person meeting the criteria for a suspected or probable case

AND

one of the following positive results conducted in a national, regional or international influenza laboratory whose H5N1 test results are accepted by WHO as confirmatory:

Confirmed Case: confirmatory test results

- Isolation of an H5N1 virus;
- Positive H5 PCR results from tests using two different PCR targets, e.g. primers specific for influenza A and H5 HA;
- A fourfold or greater rise in neutralization antibody titer for H5N1 based on testing of an acute serum specimen (collected 7 days or less after symptom onset) and a convalescent serum specimen. The convalescent neutralizing antibody titer must also be 1:80 or higher;
- A microneutralization antibody titer for H5N1 of 1:80 or greater in a single serum specimen collected at day 14 or later after symptom onset and a positive result using a different serological assay, for example, a horse red blood cell haemagglutination inhibition titer of 1:160 or greater or an H5 specific western blot positive result.

Pre-Investigation and Case Definition Activities

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2. Case Finding

Why is Case Finding Important?

- **Ensure you have identified ALL cases**
- **Case finding may provide information about human-to-human transmission**
- **Any cases related in time and space to other cases or clusters**

How to Find Cases

- **Consider all possible symptomatic persons as cases at the beginning of an investigation**
 - **Visit health facilities, homes of neighbors and adjacent communities**
 - **Public information messages in the affected communities**

Both Passive vs. Active case finding activities are important

Common Challenges to Case Finding

- **Even with case finding, all cases may not be identified**
 - **Physician may not suspect avian influenza**
 - **Some infected persons may not seek medical attention**

What are some other potential barriers to finding cases in the Eastern Province?

3. Interviewing

Who to Interview

- **Case-patient**
- **Family members/Household contacts**
- **Health care providers/Lay health workers**
- **Co-workers - if possible occupational exposure**
- **Community / Religious leaders**

Interview Tips

- **Collect as much information as possible**
 - Unstructured interviews
 - Generate list of contacts
- **Repeat critical questions for accuracy, validity and additional details**
- **On key questions, double-check information by asking different people**

Interview Tips

- **Be friendly, but professional**
- **Identify yourself and your institution**
- **Explain purpose of interview**
- **Stress importance of information you will collect**
- **Inform respondents that all information will be kept confidential**
- **If appropriate, conduct interview in private**

Type of Information to Collect

- **Demographic information: age, sex contact details**
- **Clinical information: signs & symptoms, physical exam, vitals, date of onset, hospital admission**
- **Exposure history: occupational exposure, travel, animal exposure**

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4. Specimen Collection

Confirm the Diagnosis

Specimen Collection

- **Collect safely and correctly**
- **Information needed:**
 - **Who to collect from**
 - **What samples to collect**
 - **What to wear**
 - **How to store specimens**
 - **How to transport specimens**
 - **Procedures for diagnosis**

What to Collect

Preferred specimens

- Throat swabs
- Nasal swabs
- When possible: Nasopharyngeal aspirates

Other specimens

- Posterior pharyngeal swabs
- Nasal washes
- Acute and convalescent serum

Collect the sample on several different days

Case Finding Activities

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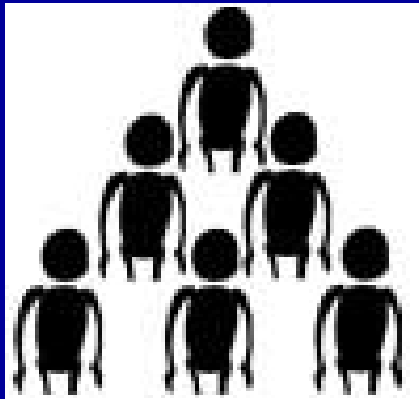


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5. Contact Identification

What is Contact Identification?

The identification and diagnosis of persons who may have come into close contact with an infected individual



Purpose of Contact Identification

- Find new cases that meet case definition
- Provide interventions for exposed individuals to decrease risk of illness and interrupt further transmission
 - Antiviral (Oseltamivir)
 - Precautionary information

Exposure (1)

q Human exposure:

§ Close contact (within 1 meter) with a probable/confirmed case of influenza A/H5N1

q Exposure to poultry and wild birds:

§ Close contact with infected birds (handling, slaughtering, defeathering, butchering, preparation for consumption) or with environments contaminated by their faeces, or consumption of raw poultry products where H5N1 infections are confirmed.

Exposure (2)

q **Exposure to other animals:**

§ **Close contact with a confirmed case of H5N1 infection in an animal**

q **Laboratory exposure:**

§ **Worked in laboratory processing samples suspected of containing A/H5 virus**

q **Reside or visit area where A(H5N1) is suspected or confirmed in birds**

Risk stratification (*)

- High risk exposure group
- Moderate risk exposure
- Low risk exposure

(*)WHO Rapid Advice Guidelines on pharmacological management of humans infected with avian influenza A(H5N1) virus

High risk exposure groups

- Household or close family contacts of a suspect, probable or confirmed H5N1 patient, because of potential exposure to a common environmental or poultry source as well as exposure to the index case

Moderate risk exposure groups

- **Personnel involved in handling sick animals or decontaminating affected environments (including animal disposal) if personal protective equipment may not have been used properly**
- **Individuals with unprotected and very close direct exposure to sick or dead animals infected with H5N1 virus**

Moderate risk exposure groups

- Health care personnel in close contact with suspect, probable or confirmed H5N1 patients (intubation , tracheal suctioning, delivery of nebulised drugs, or handling body fluids without any or with insufficient PPE.
- This group includes laboratory personnel who might have an unprotected exposure to virus containing samples.

Low risk exposure groups

- Health care workers not in close contact (> 1m) with a strongly suspected or confirmed H5N1 patient and having no direct contact with infectious material from that patient
- Health care workers who used appropriate personal protective equipment during exposure to H5N1 patients

Low risk exposure groups

- **Personnel involved in culling non infected or likely non-infected animal population as control measure**
- **Personnel involved in handling sick animals or decontaminating affected environments (including animal disposal) who used proper PPE**

How to Identify Contacts

- 1. Review patient's activities for the 7 days before onset of symptoms**
- 2. Based on activities, identify all close contacts (within 1 meter)**
- 3. Identify individuals with exposure to birds suspected to be infected with A(H5N1)**
- 4. Verify all information collected**

Key Information to Gather

- **Who** did case come into close contact with?
- **What** activities was case doing?
- **Where** did this take place?
- **When** did case come into contact with this person?

General Guidelines for Interviewing Contacts

- **Do not alarm contacts**
- **Communicate precautionary information**
- **Refer symptomatic individuals to clinic**
- **Consider if Personal Protective Equipment (PPE) is necessary**

Information to Gather from Contact

- **Demographic and contact information**
 - Name, Address
 - Occupation, age, gender
- **Exposure History**
 - Contact with case-patient
 - Poultry and wild bird exposure
 - Other high-risk exposures
- **Physical Exam and Clinical information**
 - Health status
 - Temperature
 - Presence of sore throat, coughing
 - Signs and symptoms

Monitoring and Managing Contacts

- **Monitor for signs of illness for at least 7 days after contact with case or potentially infected birds**
 - Encourage self-health monitoring
 - Instruct to report onset of symptoms
 - Visit or phone daily to monitor for illness
- **Request voluntary home quarantine of all contacts for at least 7 days**
- **Consider antiviral prophylaxis**

Prioritize Contact Identification

- If number of contacts is large focus on:
 - Contacts of laboratory confirmed cases
 - Contacts with extended duration and closeness to case
 - Contacts that are at high risk
 - those involved in unprotected care of case
 - those with exposure to birds suspected of being infected with A(H5N1)
 - Contacts from large gatherings and/or school that case attended

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6. Reporting: Informing 'Those who Need to Know'

Inform 'Those who Need to Know'

- **Local Level** Who is responsible for submitting AI case reports? When should this be done?
- **National Level** Who needs to be updated on the progress of the investigation and receive the final report on number of cases? Who is responsible for assuring that this occurs?
- **International Level** What international agencies need to be informed of suspect human cases? Who in your country is responsible for notifying international authorities?

How and When to Report

- **Use standard reporting forms**

(Case/Lab specimen based, line-lists, Weekly, IDS Monthly, Contacts follow-up forms, Outbreak report form: cf IDSR technical guidelines and addenda)

- **Immediate, weekly reporting of cases/clusters to next levels**

- **Information flow**

- through early warning system by fastest possible means
- Information should be shared both vertically (reporting and feedback) and horizontally

- **Notification according to IHR (2005) =
Immediately**

Inform 'Those who Need to Know'

- **International Health Regulations (IHR)**
 - Compulsory notification of highly-pathogenic strains of avian influenza
 - Vaccination and food safety of poultry products
- **Compliance with these standards is required to strengthen early detection, reporting, and response**

Contact Identification and Reporting Activities

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7. Managing Data on Cases and Contacts

Data Management

- **Line listing**
- **Record keeping**
- **Validation and Cross-Checking**

Example of Line Listing

An organized way to view all cases in an investigation

| Case # | Age | Sex | Status | Occupation | Difficult breathing | Date of Onset |
|--------|-----|-----|----------|----------------------|---------------------|---------------|
| 1 | 5 | M | Probable | Child | Yes | 7 July |
| 2 | 55 | F | Suspect | Caretaker of case #1 | Yes | 9 July |
| 3 | 48 | M | Suspect | Poultry Farmer | No | 7 July |

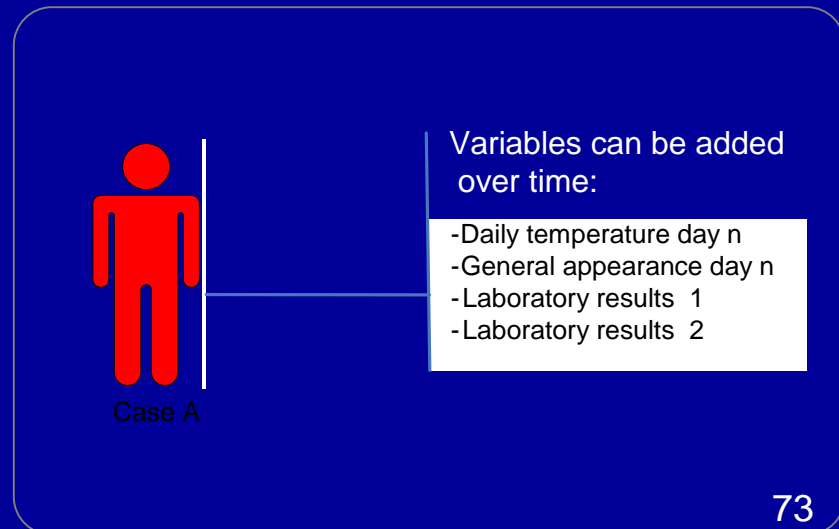
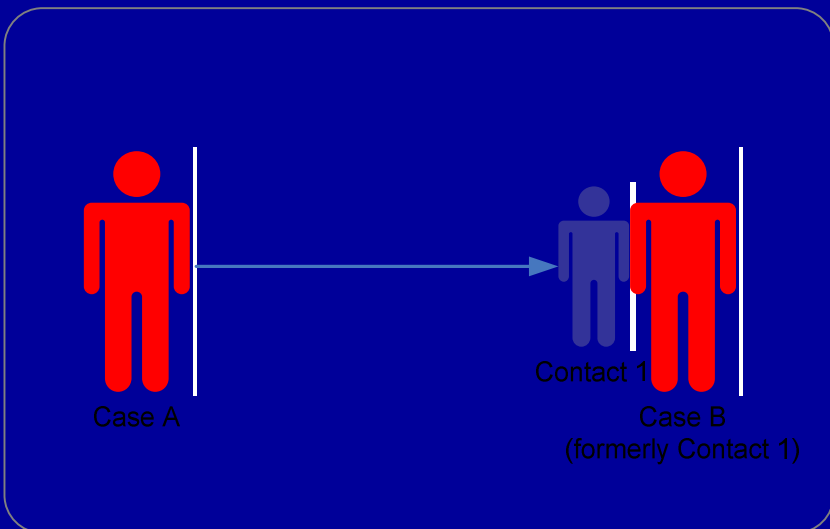
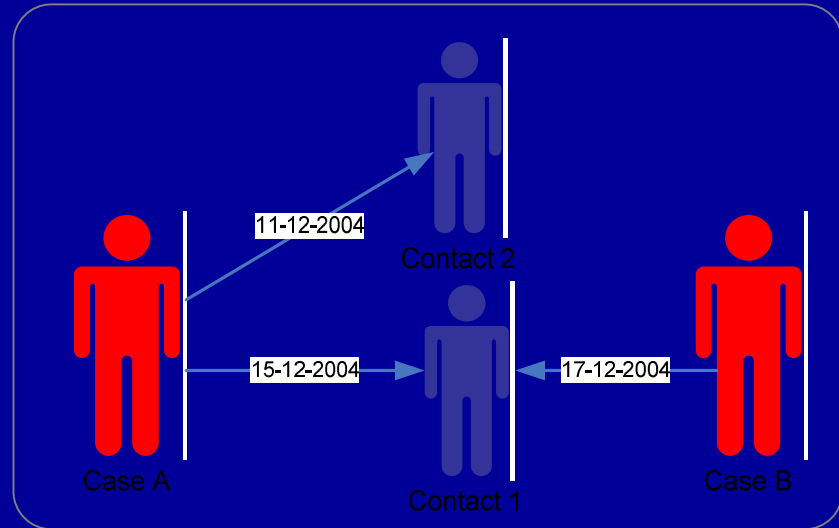
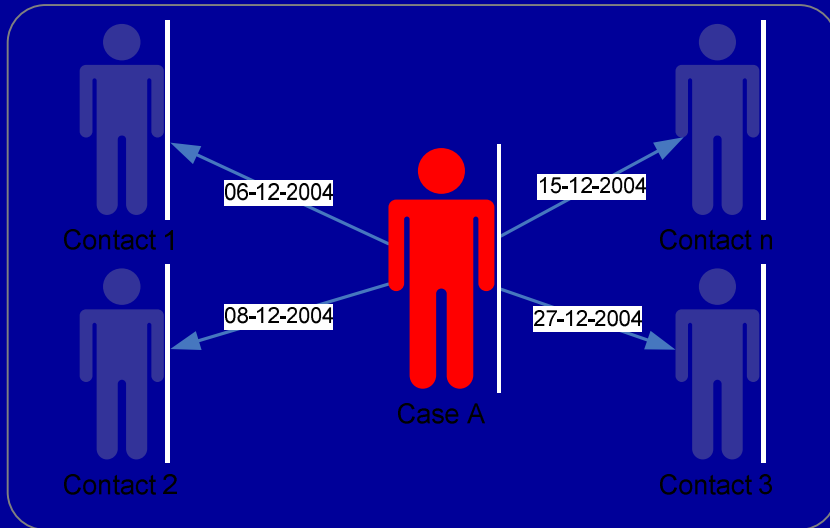
Information included:

- Demographic
- Clinical
- Exposure

Record Keeping

- **Keep track of cases and contacts**
 - Links between cases and contacts
 - Duration of follow up
 - Monitoring of follow up activities
- **Maintain confidentiality**
- **Assigned someone to data management and record keeping**
- **Software**

Managing different scenarios



Validation and Cross-Checking

- **Check line lists against medical charts and interviews**
- **Validation**
 - Ask same question in different ways
 - Ask same question at different times
 - Ensure answers are consistent

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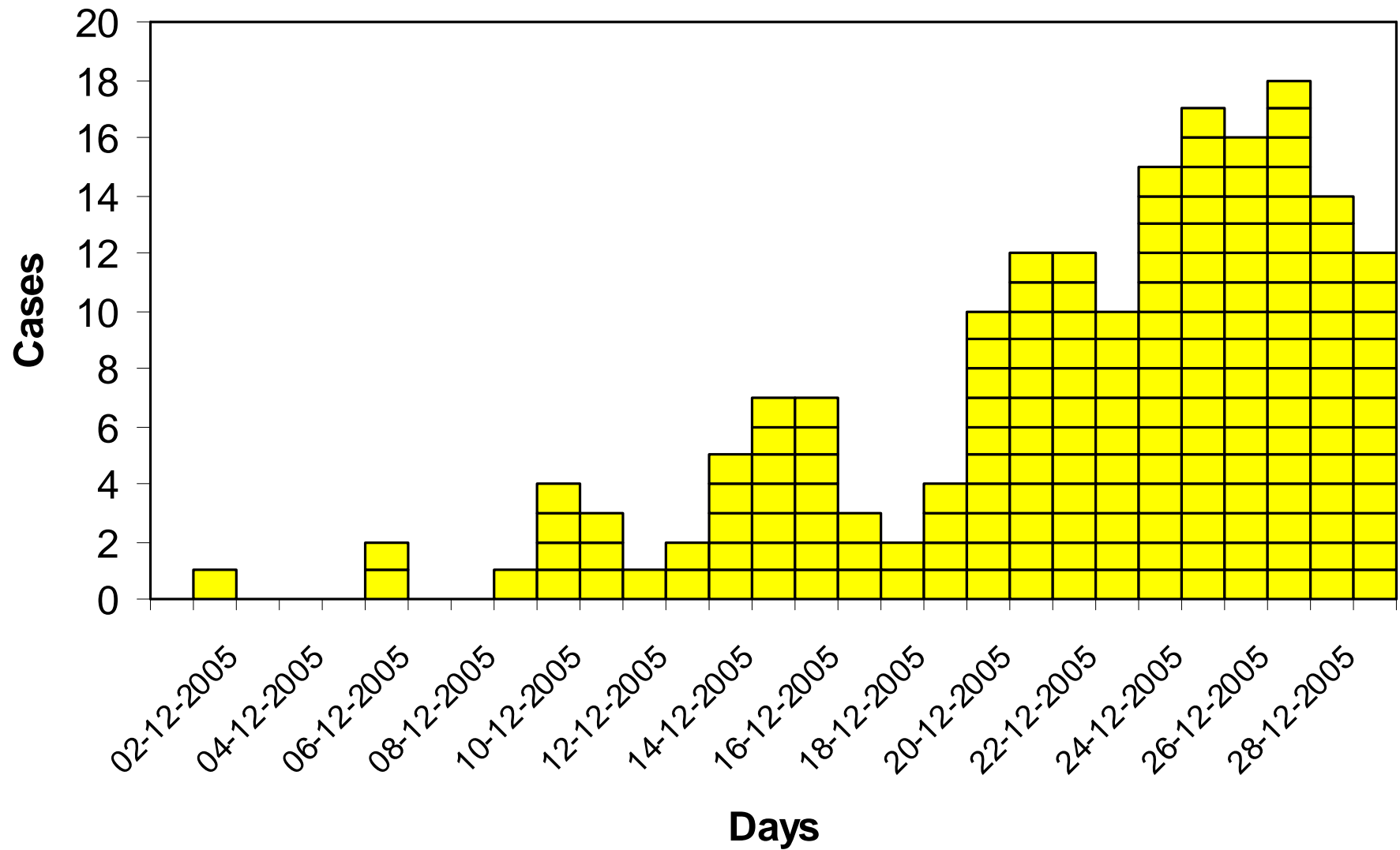


8. Depicting data

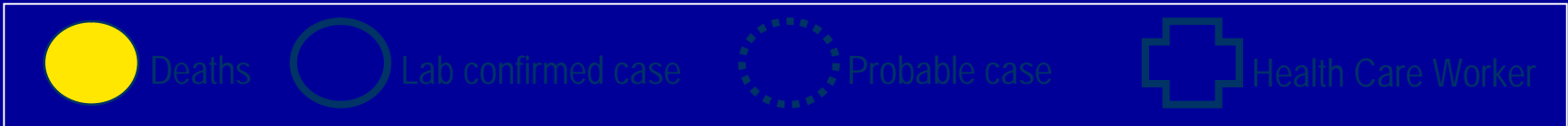
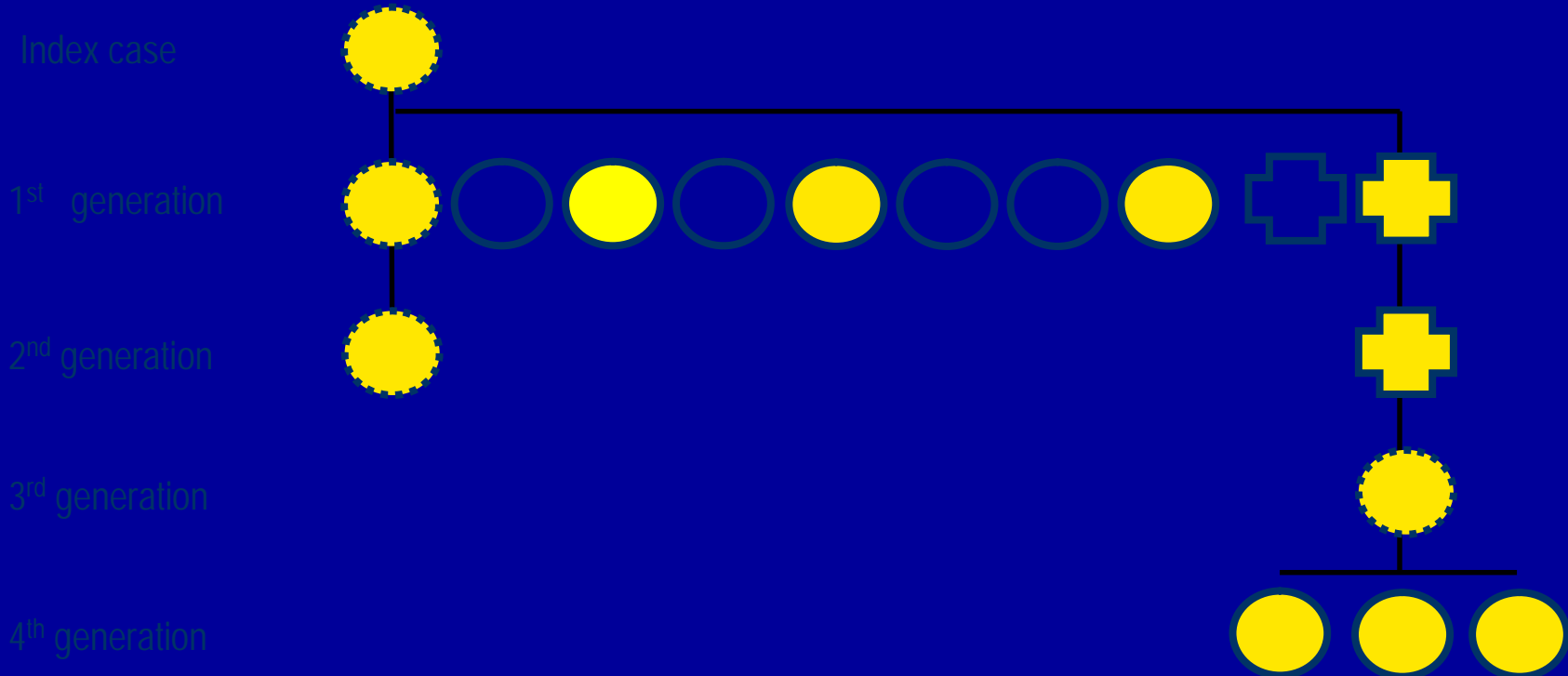
Epidemic Curve

- **Provides information characteristics of an outbreak:**
 - Magnitude
 - Pattern of spread
 - Outliers (case outside expected time frame)
 - Time trend
 - Disease incubation period

Number of cases of X per day



Transmission tree



Data Management and Epidemic Curve Activities

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9. Assessing Human to Human Transmission

Current Status of H5N1 Transmission

- **Now**
 - Human-to-human transmission of Influenza A/H5 highly ineffective
 - Has occurred only among very close contacts
- **In the future**
 - Virus could mutate and pass between humans
 - Global outbreak could occur

Assessing Human to Human Transmission

- **Cases occur close together in time and place among individuals who had close contact with a human case**
 - Family members or health care workers
- **Onset between two cases falls within the incubation period**
- **No alternative source of exposure is found**

When a Cluster May Exist

- **3 or more people with moderate or severe acute respiratory illness**
 - Unexplained by other causes
 - May have died from the illness
 - Onset within 7-10 days of each other

AND

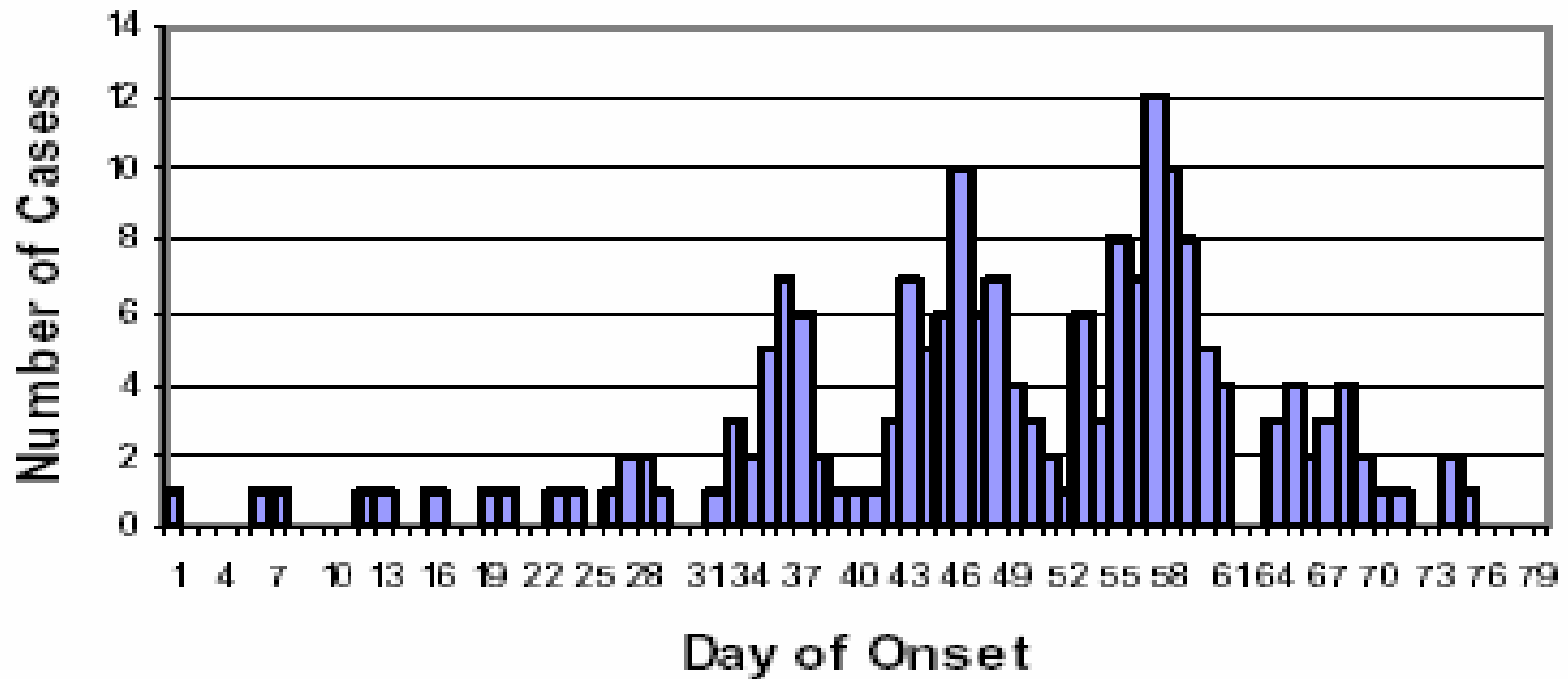
- **History strongly suggesting exposure to H5N1 virus**

Epidemic Curves and Transmission

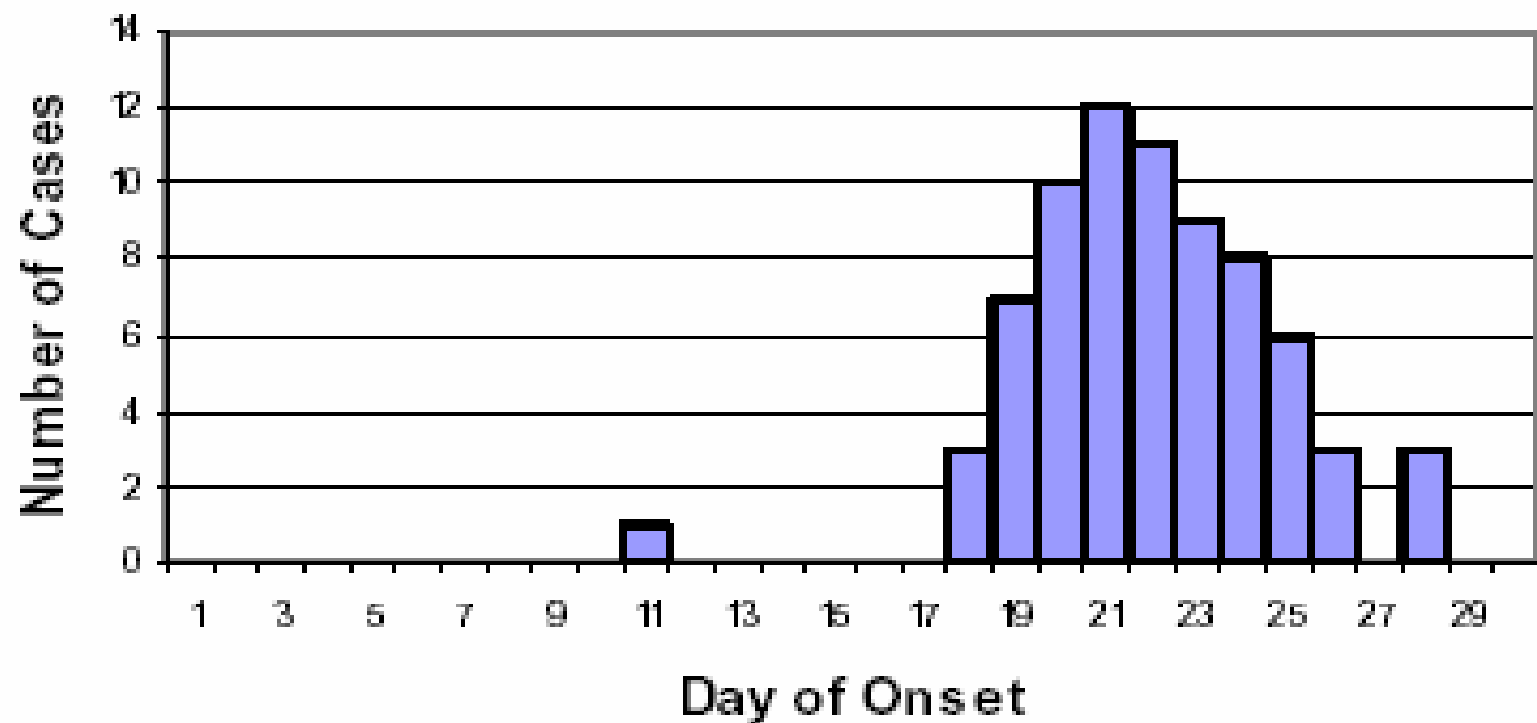
Assess whether human-to-human transmission is occurring

- Epi curve pattern for infectious agent transmitted between people
- Epi curve pattern for infectious agent transmitted from one source to people

Example Epi Curve for Human to Human Transmission



Example Epi Curve for Human Cases from Single Source



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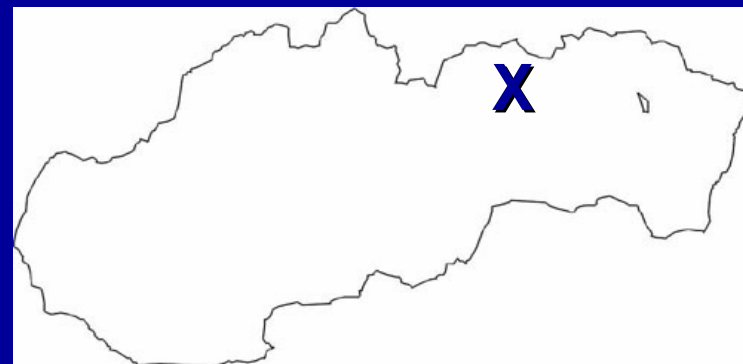


Case Study Conclusion

Outbreak Ends in Eastern

1 September 2006

- H5N1 cases identified = 6
- RRT interviewed 52 possible case contacts
 - 96% of these received antiviral prophylaxis
- Deaths = 5
- Case Fatality Rate = 83%



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10. Writing a Summary Report

Why communicate the findings?

- **A document for action**
 - **Control and prevention measures**
- **To share new insights**
- **Documents the investigation**
- **To assist other nations districts or countries with investigation**
- **Inform the public**
 - **Prevents future outbreaks**

Content of a Summary Report

- **Summary**
- **Introduction and Background**
- **Outbreak Description**
- **Methods and Results**
- **Discussion**
- **Lessons Learned**
- **Recommendations**
- **Acknowledgements**
- **Supporting Documentation**

Human-to-Human Transmission and Summary Report Activities